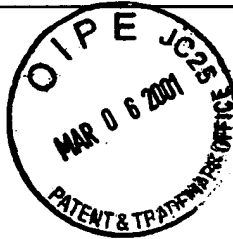



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Patent Docket P1093P1D1

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of Manuel Baca et al. Serial No.: 09/723,752 Filed: November 27, 2000 For: ANTI-VEGF ANTIBODIES	 Group Art Unit: Examiner: CERTIFICATE OF MAILING I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Assistant Commissioner of Patents, Washington, D.C. 20231 on February 28, 2001  Eileen Ly
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INFORMATION DISCLOSURE STATEMENT

Assistant Commissioner of Patents
Washington, D.C. 20231

Sir:

Applicants submit herewith patents, publications or other information (attached hereto and listed on the attached revised Form PTO-1449) of which they are aware, which they believe may be material to the examination of this application and in respect of which there may be a duty to disclose in accordance with 37 CFR §1.56.

This Information Disclosure Statement is filed in accordance with the provisions of:

☒ **37 CFR §1.97(b)**

- within three months of the filing date of the application other than a continued prosecution application under 37 CFR §1.53(d); or
- within three months of the date of entry of the national stage of a PCT application as set forth in 37 CFR §1.491, or
- before the mailing of the first Office action on the merits; or
- before the mailing of the first Office action after the filing of a request for a continued examination under 37 CFR §1.114.

☐ **37 CFR §1.97(c)**

- by the applicant after the period specified in 37 CFR §1.97(b), but prior to the mailing date of any of a final action under 37 CFR §1.113, or a notice of allowance under 37 CFR §1.311, or an action that otherwise closes prosecution in the application, and is accompanied by either the fee set forth in 37 CFR §1.17(p) or a statement as specified in 37 CFR §1.97(e), as checked below.

☐ **37 CFR §1.97(d)**

- after the period specified in CFR §1.97(c), and is accompanied by the fee set forth in 37 CFR §1.17(p) and a statement as specified in 37 CFR §1.97(e), as checked below.

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[If either of boxes 37 CFR §1.97(c) or 37 CFR §1.97(d) is checked above, the following statement under 37 CFR §1.97(e) may need to be completed.]

- ☐ **37 CFR §1.97(e)** Each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of this information disclosure statement.
- ☐ **37 CFR §1.704(d)** Each item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application and the communication was not received by any individual designated in §1.56(c) more than thirty days prior to the filing of this information disclosure statement. Therefore, in accordance with the provisions of 37 CFR §1.704(d), the filing of this information disclosure statement will not be considered a failure to engage in reasonable efforts to conclude prosecution under 37 CFR §1.704.
- ☐ The U.S. Patent and Trademark Office is hereby authorized to charge Deposit Account No. 07-0630 in the amount of \$180.00 to cover the cost of this Information Disclosure Statement under 37 CFR §1.17(p). Any deficiency or overpayment should be charged or credited to this deposit account.

A list of the patent(s) or publication(s) is set forth on the attached revised Form PTO-1449 (Modified). Those patent(s) or publication(s) which are marked with an asterisk (*) in the attached PTO-1449 form are not supplied because they were previously cited by or submitted to the Office in a prior application Serial No. 08/908,469, filed August 6, 1997 and relied upon in this application for an earlier filing date under 35 USC §120.

☐ BLAST results enclosed:

The undersigned also wishes to bring to the attention of the Examiner BLAST results of computerized alignments of the against sequences contained in the nucleotide and protein databases. The BLAST results are provided in paper form and are identified as reference "BLAST Results A-1- A-()" (nucleotide) and "BLAST Results B-1 - B-()" (protein) on the PTO Form 1449. Applicant requests that these references also be considered and that the Form 1449 be initialed to indicate the Examiner's consideration of the references.

A concise explanation of relevance of the items listed on PTO-1449 is:

☒ not given

☐ given for each listed item

☐ given for only non-English language listed item(s) [Required]

☐ in the form of an English language copy of a Search Report from a foreign patent office, issued in a counterpart application, which refers to the relevant portions of the references.

In accordance with 37 CFR §1.97(g), the filing of this information disclosure statement shall not be construed as a representation that a search has been made.

In accordance with 37 CFR §1.97(h), the filing of this information disclosure statement shall not be construed to be an admission that the information cited in the statement is, or is considered to be, material to patentability as defined in 37 CFR § 1.56(b).

In the event that the Office determines a fee to be due where none is specifically authorized in this paper, the U.S. Patent and Trademark Office is hereby authorized to charge Deposit Account No. 07-0630 in the amount of \$180.00 to cover the cost of this Information Disclosure Statement under 37 CFR §1.17(p).

Respectfully submitted,

GENENTECH, INC.

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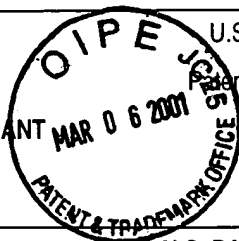
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Serial No.

09/723752

LIST OF DISCLOSURES CITED BY APPLICANT

(Use several sheets if necessary)



Applicant

Baca et al.

Filing Date

27 Nov 2000

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U.S. PATENT DOCUMENTS

Examiner Initials		Document Number	Date	Name	Class	Subclass	Filing Date
	* 1	4,816,567	28.03.89	Cabilly et al.			
	* 2	5,530,101	25.06.96	Queen et al.			19.12.90
	* 3	5,580,723	01.12.96	Wells et al.			

FOREIGN PATENT DOCUMENTS

Examiner Initials		Document Number	Date	Country	Class	Subclass	Translation Yes No
	* 4	0,451,216	01.01.96	EPO			
	* 5	WO 91/09967	11.07.91	PCT			
	* 6	WO 92/22653	23.12.92	PCT			
	* 7	WO 94/04679	03.03.94	PCT			
	* 8	WO 94/10202	11.05.94	PCT			
	* 9	WO 96/30046	03.10.96	PCT			
	*10	2,268,744	19.12.94	UNITED KINGDOM			
	*11	2188638	07.10.87	UNITED KINGDOM			

OTHER DISCLOSURES (Including Author, Title, Date, Pertinent Pages, etc.)

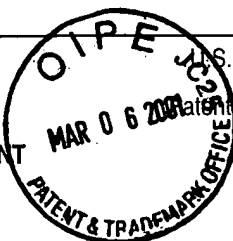
	*12	Adamis et al., "Inhibition of Vascular Endothelial Growth Factor Prevents Retinal Ischemia-Associated Iris Neovascularization in a Nonhuman Primate" <u>Arch. Ophthalmology</u> 114(1):66-71 (1996)				
	*13	Aiello et al., "Vascular endothelial growth factor in ocular fluid of patients with diabetic retinopathy and other retinal disorders" <u>New England J. of Medicine</u> 331(22):1480-1487 (1994)				
	*14	Alberts et al., "Molecular Biology of the Cell", 3rd edition, Garland Publishing pps. 1154 (1994)				
	*15	Allen et al., "Specificity of the T cell Receptor: Two Different Determinants are Generated by the Same Peptide and the IAK Molecule" <u>J. Immunol.</u> 135(1):368-373 (Jul 1985)				
	*16	Baca et al., "Antibody Humanization Using Monovalent Phage Display" <u>Journal of Biological Chemistry</u> 272(16):10678-10684 (1997)				
	*17	Bass et al., "Hormone Phage: An Enrichment Method for Variant Proteins with Altered Binding Properties" <u>Proteins: Structure, Function, and Genetics</u> 8(4):309-314 (1990)				
	*18	Bendig, M. M., "Humanization of Rodent Monoclonal Antibodies" <u>Methods: A Companion to Methods in Enzymology</u> 8:83-93 (1994)				
	*19	Berkman et al., "Expression of the vascular permeability factor/vascular endothelial growth factor gene in central nervous system neoplasms" <u>J. Clin. Invest.</u> 91(1):153-159 (1993)				
	*20	Borgstrom et al., "Complete inhibition of angiogenesis and growth of microtumors by anti-vascular endothelial growth factor neutralizing antibody: novel concepts of angiostatic therapy from intravital videomicroscopy" <u>Cancer Research</u> 56(17):4032-4039 (1996)				
	*21	Brown et al., "Expression of vascular permeability factor (vascular endothelial growth factor) and its receptors in adenocarcinomas of the gastrointestinal tract" <u>Cancer Research</u> 53(19):4727-4735 (1993)				
	*22	Brown et al., "Expression of vascular permeability factor (vascular endothelial growth factor) and its receptors in breast cancer" <u>Human Pathology</u> 26(1):86-91 (1995)				

Examiner

Date Considered

*Examiner: Initial if reference considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

FORM PTO-1449

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OTHER DISCLOSURES (Including Author, Title, Date, Pertinent Pages, etc.)

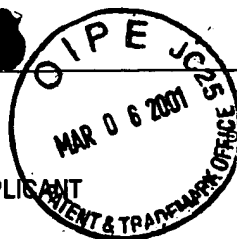
*23	Carter et al., "Humanization of an anti-p185 ^{HER2} antibody for human cancer therapy" <u>Proc. Natl. Acad. Sci.</u> 89:4285-4289 (1992)
*24	Chang et al., "High-level secretion of human growth hormone by Escherichia coli" <u>Gene</u> 55:189-196 (1987)
*25	Chisholm, "High Efficiency Gene Transfer into Mammalian Cells" <u>DNA Cloning</u> 4: Mammalian Systems pps. 1-41 (1995)
*26	Chothia et al., "Domain Association in Immunoglobulin Molecules. The Packing of Variable Domains" <u>Journal of Molecular Biology</u> 186:651-663 (1985)
*27	Clapp et al., "The 16-kilodalton N-terminal fragment of human prolactin is a potent inhibitor of angiogenesis" <u>Endocrinology</u> 133(3):1292-1299 (1993)
*28	Cunningham et al., "Production of an Atrial Natriuretic Peptide Variant that is Specific for Type A Receptor" <u>EMBO Journal</u> 13(11):2508-2515 (1994)
*29	de Vries et al., "The fms-like tyrosine kinase, a receptor for vascular endothelial growth factor" <u>Science</u> 255:989-991 (1992)
*30	Dvorak et al., "Vascular permeability factor/vascular endothelial growth factor, microvascular hyperpermeability, and angiogenesis" <u>American Journal of Pathology</u> 146(5):1029-1039 (1995).
*31	Eaton et al., "Construction and characterization of an active factor VIII variant lacking the central one-third of the molecule" <u>Biochemistry</u> 25:8343-8347 (1986)
*32	Eigenbrot et al., "X-Ray Structures of Fragments From Binding and Nonbinding Versions of a Humanized Anti-CD18 Antibody: Structural Indications of the Key Role of V _H Residues 59 to 65" <u>Proteins: Structure, Function, and Genetics</u> 18:49-62 (1994)
*33	Eigenbrot et al., "X-ray structures of the antigen-binding domains from three variants of humanized anti-p185 ^{HER2} antibody 4D5 and comparison with molecular modeling" <u>J. Mol. Biol.</u> 229:969-995 (1993)
*34	Ferrara and Davis-Smyth, "The biology of vascular endothelial growth factor" <u>Endocrine Reviews</u> 18(1):4-25 (1997)
*35	Folkman and Shing, "Angiogenesis" <u>Journal of Biological Chemistry</u> 267:10931-10934 (1992)
*36	Foote et al., "Antibody Framework Residues Affecting the Conformation of the Hypervariable Loops" <u>J. Mol. Biol.</u> 224:487-499 (1992)
*37	Garner, A., "Vascular Diseases" <u>Pathobiology of Ocular Disease. A Dynamic Approach</u> , Garner, A., Klintworth GK Eds., 2nd edition, NY:Marcel Dekker pps. 1625-1710 (1994)
*38	Garrard et al., "Fab assembly and enrichment in a monovalent phage display system" <u>Bio/technology</u> 9:1373-1377 (1991)
*39	Good et al., "A tumor suppressor-dependent inhibitor of angiogenesis is immunologically and functionally indistinguishable from a fragment of thrombospondin" <u>Proc. Natl. Acad. Sci. USA</u> 87(17):6624-6628 (1990)
*40	Gorman et al., "Transient Production of Proteins Using an Adenovirus Transformed Cell Line" <u>DNA Prot. Eng. Tech.</u> 2(1):3-10 (1990)
*41	Graham et al., "Characteristics of a Human Cell Line Transformed by DNA from Human Adenovirus Type 5" <u>J. Gen. Virol.</u> 36:59-74 (1977)
*42	Hawkins et al., "Selection of Phage Antibodies by Binding Affinity Mimicking Affinity Maturation" <u>J. Mol. Biol.</u> 226:889-896 (1992)

Examiner

Date Considered

*Examiner: Initial if reference considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

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27 Nov 2000

Group

LIST OF DISCLOSURES CITED BY APPLICANT

(Use several sheets if necessary)

OTHER DISCLOSURES (Including Author, Title, Date, Pertinent Pages, etc.)

*43	Horak et al., "Angiogenesis, assessed by platelet/endothelial cell adhesion molecule antibodies, as indicator of node metastases and survival in breast cancer" <u>Lancet</u> 340(8828):1120-1124 (1992)
*44	Kabat et al. <u>Sequences of Proteins of Immunological Interest</u> , U.S. Dept. of Health and Human Services, NIH, 5th edition Vol. 1:103-108, 324-331 (1991)
*45	Karlsson et al., "Kinetic analysis of monoclonal antibody-antigen interactions with a new biosensor based analytical system" <u>J. Immun. Methods</u> 145:229-240 (1991)
*46	Karlsson et al., "Kinetic and Concentration Analysis Using BIA Technology" <u>Methods: A Comparison to Methods in Enzymology</u> 6:99-110 (1994)
*47	Kettleborough et al., "Humanization of a Mouse Monoclonal Antibody by CDR-grafting: the Importance of Framework Residues on Loop Conformation" <u>Protein Engineering</u> 4(7):773-783 (1991)
*48	Kim et al., "Inhibition of Vascular Endothelial Growth Factor-Induced Angiogenesis Suppresses Tumour Growth in vivo" <u>Nature</u> 362:841-844 (1993)
*49	Kim et al., "The Vascular Endothelial Growth Factor Proteins: Identification of Biologically Relevant Regions by Neutralizing Monoclonal Antibodies" <u>Growth Factors</u> 7(1):53-64 (1992)
*50	Klagsbrun and D'Amore, "Regulators of angiogenesis" <u>Ann. Rev. Physiol.</u> 53:217-239 (1991)
*51	Kunkel et al., "Efficient site-directed mutagenesis using uracil-containing DNA" <u>Methods in Enzymology</u> 204:125-139 (1991)
*52	Kunkel, T., "Rapid and Efficient Site-Specific Mutagenesis Without Phenotypic Selection" <u>Proc. Natl. Acad. Sci.</u> 82:488-492 (1985)
*53	Leung et al., "Vascular Endothelial Growth Factor is a Secreted Angiogenic Mitogen" <u>Science</u> 246:1306-1309 (1989)
*54	Lopez et al., "Transdifferentiated retinal pigment epithelial cells are immunoreactive for vascular endothelial growth factor in surgically excised age-related macular degeneration-related choroidal neovascular membranes" <u>Invest. Ophthalmol. Vis. Sci.</u> 37(5):855-868 (1996)
*55	Lowman et al., "Selecting High-Affinity Binding Proteins by Monovalent Phage Display" <u>Biochemistry</u> 30(45):10832-10838 (1991)
*56	Lucas et al., "High-level production of recombinant proteins in CHO cells using a dicistronic DHFR intron expression vector" <u>Nucleic Acids Research</u> 24(9):1774-1779 (1996)
*57	Macchiarini et al., "Relation of neovascularisation to metastasis of non-small-cell lung cancer" <u>Lancet</u> 340(8812):145-146 (1992)
*58	Mattern et al., "Association of vascular endothelial growth factor expression with intratumoral microvessel density and tumour cell proliferation in human epidermoid lung carcinoma" <u>Brit. J. Cancer</u> 73(7):931-934 (1996)
*59	Melnyk et al., "Vascular endothelial growth factor promotes tumor dissemination by a mechanism distinct from its effect on primary tumor growth" <u>Cancer Research</u> 56(4):921-924 (1996)
*60	Novotny et al., "Structural invariants of antigen binding: comparison of immunoglobulin V _L -V _H and V _L -V _L domain dimers" <u>Proc. Natl. Acad. Sci. USA</u> 82(14):4592-4596 (Jul 1985)
*61	O'Reilly et al., "Angiostatin: a novel angiogenesis inhibitor that mediates the suppression of metastases by a Lewis lung carcinoma" <u>Cell</u> 79(2):315-328 (1994)
*62	O'Reilly et al., "Endostatin: an endogenous inhibitor of angiogenesis and tumor growth" <u>Cell</u> 88(2):277-285 (1997)

Examiner

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*Examiner: Initial if reference considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

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(Use several sheets if necessary)

Applicant

Baca et al.

Filing Date

27 Nov 2000

Group

OTHER DISCLOSURES (Including Author, Title, Date, Pertinent Pages, etc.)

*63	Padlan, E., "A Possible Procedure for Reducing the Immunogenicity of Antibody Variable Domains While Preserving Their Ligand-Binding Properties" <u>Molecular Immunology</u> 28(4/4):489-498 (1991)
*64	Park et al., "Placenta growth factor. Potentiation of vascular endothelial growth factor bioactivity, in vitro and in vivo, and high affinity binding to Flt-1 but not to Flk-1/KDR" <u>Journal of Biological Chemistry</u> 269(41):25646-25654 (1994)
*65	Presta et al., "Humanization of an Antibody Directed Against IgE" <u>J. Immunol.</u> 151(5):2623-2632 (September 1, 1993)
*66	Queen et al., "A humanized antibody that binds to the interleukin 2 receptor" <u>Proc. Natl. Acad. Sci. USA</u> 86(24):10029-10033 (December 1989)
*67	Roguska et al., "Humanization of murine monoclonal antibodies through variable domain resurfacing" <u>Proc. Natl. Acad. Sci. USA</u> 91:969-973 (Feb 1994)
*68	Rosok et al., "A Combinatorial Library Strategy for the Rapid Humanization of Anticarcinoma BR96 Fab" <u>Journal of Biological Chemistry</u> 271(37):22611-22618 (Sep 13, 1996)
*69	Sanger et al., "DNA Sequencing with Chain-terminating Inhibitors" <u>Proc. Natl. Acad. Sci. USA</u> 74(12):5463-5467 (Dec 1977)
*70	Shalaby et al., "Development of Humanized Bispecific Antibodies Reactive with Cytotoxic Lymphocytes and Tumor Cells Overexpressing the HER2 Protooncogene" <u>Journal of Experimental Medicine</u> 175:217-225 (Jan 1, 1992)
*71	Studnicka et al., "Human-engineered monoclonal antibodies retain full specific binding activity by preserving non-CDR complementarity-modulating residues" <u>Protein Eng.</u> 7(6):805-814 (1994)
*72	Tempest et al., "Reshaping a Human Monoclonal Antibody to Inhibit Human Respiratory Syncytial Virus Infection In Vivo" <u>Bio/Technology</u> 9:266-271 (March 1991)
*73	Vieira et al., "Production of Single-stranded Plasmid DNA" <u>Methods in Enzymology</u> 153:3-11 (1987)
*74	Warren et al., "Regulation by vascular endothelial growth factor of human colon cancer tumorigenesis in a mouse model of experimental liver metastasis" <u>J. Clin. Invest.</u> 95(4):1789-1797 (1995)
*75	Weidner et al., "Tumor angiogenesis and metastasis--correlation in invasive breast carcinoma" <u>New England J. of Medicine</u> 324(1):1-8 (1991)
*76	Werther et al., "Humanization of an Anti-Lymphocyte Function-Associated Antigen (LFA)-1 Monoclonal Antibody and Reengineering of the Humanized Antibody for Binding to Rhesus LFA-1" <u>J. of Immunology</u> 157:4986-4995 (1996)
*77	Winter et al., "Making antibodies by phage display technology" <u>Annual Review of Immunology</u> 12:433-455 (1994)
*78	Yang et al., "CDR walking mutagenesis for the affinity maturation of a potent human anti-HIV-1 antibody into the picomolar range" <u>Journal of Molecular Biology</u> 254(3):392-403 (Dec 1, 1995)

Examiner

Date Considered

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